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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/488,298	01/20/2000	Olivier Lutz	3874-128 US	4242

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08/26/2003

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EXAMINER

KIM, JENNIFER M

ART UNIT

PAPER NUMBER

1617

DATE MAILED: 08/26/2003

27

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/488,298

Applicant(s)

LUTZ ET AL.

Examiner

Jennifer Kim

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 June 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4 and 7-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 4, 7-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

The amendment filed June 5, 2003 have been received and entered into the application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1,18, 20 and 21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The proviso that "free tocoferol is not present" lack literal support in the specification as filed. This is New Matter rejection.

It is suggested to amend claims drawn to "consisting of" in order to overcome instant rejection.

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The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7, 8, 10 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "derivative" renders the claims vague and indefinite since it is not clear what are the physical or chemical characteristics that satisfies for the term "derivatives". One of ordinary skill in the art would not be able to determine what "derivatives" of the compounds to be utilized to practice the Applicants' invention since there is no metes and bounds of the term "derivatives" in the specification as filed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 4 and 7-24 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Lambert et al. (U.S. Patent No. 6,458,373B1) is maintained for the reasons stated in the previous office action.

Response to Arguments

Applicants' arguments filed June 5, 2003 and the declaration of Dr. Valery Alakhov has been fully considered but they are not persuasive.

Applicants argue that the formulations contemplated by Lambert, et al, in the U.S. Patent No. 6,458,373 all requires **free tocopheral** and are particularly developed, intended and preferred for the administration of Paclitaxel as a hydrophobic therapeutic agent. This is not persuasive because Applicants amended claims drawn to the limitation of "the **proviso that free tocoferol is not present**" lack literal support in the specification as filed and therefore it is New Matter. Further, Applicants' attention is drawn to the Example 23 of Lambert et al. where it teaches specific example of the pharmaceutical formulation comprising Etoposide and TPGS. Therefore this working example clearly indicates the intended and preferred administration of Applicants' active agent etoposide in a formulation. Applicants next argue that the Applicants' defined compositions and methods of treatment merely require a podophyllotoxin and tocopherol covalently linked to a water-soluble polymer and as demonstrated by the Applicants and in contrast to the suggestion of Lambert et al. disclosure, ionic and non-ionic surfactants, POLOXAMERS for example, PLURONIC P85, PLURONIC 127, PLURONIC 123, PLURONIC 68, PLURONIC 108,88,61, polyethyleneimine-polyoxyethylene do not solubilized podophyllotoxin, and are in fact detrimental to the efficacy of podophyllotoxin pharmaceutical composition. See, e.g. Applicants'

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Examples IV-XII, Specification pages 35-38. This is not persuasive because the Examples IV-XII of the specification pages 35-38 do not consists of TPGS which is required by the prior art (Examples) and the instant claims. It is noted that the comparative evidence, to be effective, must compare the claimed subject matter with the closest prior art. Applicants further argue that the formulations taught by the Applicants are physically and pharmacologically functional and exhibits significantly greater efficacy than the currently available accepted clinical standard. As evidence of the nonobviousness of the claimed invention, Applicants puts forth the Declaration under 37 CFR 1.132 suggesting, and providing evidence, that the addition of alpha-tocopherol (free tocopherol) to formulation comprising Etoposide and TPGS dramatically reduces the solubility of Etoposide and lead to phase separation. However, Applicants are reminded that when relying on comparative testing, the Applicants are under a duty of compare his claimed invention with the closest prior art (i.e. Example 23 (Col. 21) of Lambert et al.). Applicants' Declaration does not indicate how the composition tested related to the composition disclosed in Lambert et al. (Example 23), and thus, it does not appear that Applicants have compared the claimed method and the composition with that of the closest prior art. Thus, the claims fail to patentably distinguish over the state of the art as represented by the cited references.

None of the claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Kim whose telephone number is 703-308-2232. The examiner can normally be reached on Monday through Friday 8:30am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 703-305-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.



Sreenivasan Padmanabhan
Supervisory Examiner
Art Unit 1617

8/25/03

jmk